"Synthesis, Chemistry and Characterization of New Fused Heterocyclic Compounds and Study of Their Biological Properties"

SHORT RESUME OF THE PLAN PROPOSED FOR INVESTIGATION FOR Ph.D. DEGREE UNDER THE FACULTY OF SCIENCE.

To be submitted to

Swami Ramanand Teerth Marathwada University, Nanded

By

Mrs. Archana P. Mitake
(Research Scholar)
Dept. of Chemistry,
Yeshwant Mahavidyalaya, Nanded-431602.

Under the Guidance of

Dr. Sambhaji. P. Vartale
(Research Guide)
Professor
P.G. Research Center,
Dept. of Chemistry,
Yeshwant Mahavidyalaya, Nanded-431602

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1. Introduction:

Heterocyclic compounds and their derivatives have been widely used in agronomy and medicine because of their unique biological activity, which is used in many biological fields, like Pharmaceuticals, agrochemical and veterinary product due to it is an activity in multiple illnesses. Biological molecules such as DNA and RNA, chlorophyll, hemoglobin, vitamins and many more contains the heterocyclic ring in the major skeleton. There are a lot of heterocyclic compounds which have application in many common diseases such as; triazine derivatives have been used as antimicrobial herbicides, urinary antiseptics, and anti-inflammatory agents. Benzimidazole derivatives have been reported to possess a wide range of biological activities such as antibacterial, antifungal, antiviral, and anthelmintic, etc.

Heterocyclic compounds shows broad existence in nature, particularly in biological systems like nucleic acids, hemoglobin, plant, hormones and enzymes. Organic synthesis is one of the special branch in chemical synthesis and is concerned with the construction of organic compounds by reactions. It is believed to be one of the most vital roles in organic chemistry because of the organic molecules used to contain higher level of complexity compared to pure inorganic compounds. So far, organic synthesis plays a very significant role in many sectors such as pharmaceuticals, agricultural and others.

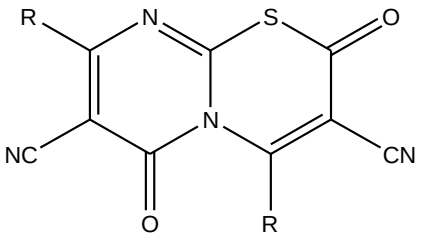
2. Review of Literature and Development in the subject (Previous work done in the relevant area):

Now we are working on the development of the Nitrogen, Sulphur containing fused heterocyclic compounds by applying different catalytic reagents. Some of them have been mentioned below.

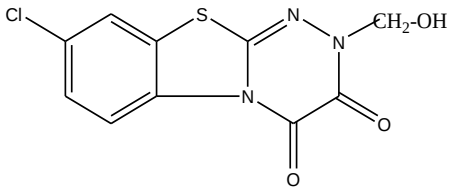
The present work with our research group involves the synthesis of novel biological active fused heterocycles containing imino /oxo pyrimdine ring fused through the nitrogen atom with another biologically active nucleus such as Pyridine,

Imidazole pyrazole, thiazole, benzothiazole, and quinolines which are published in different reputed journals.

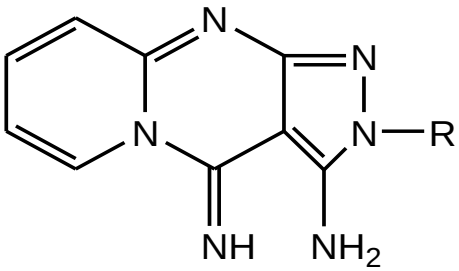
- Simple and efficient synthesis of substituted pyrimido [2,1-*b*][1,3] thiazines, Sambhaji P. Vartale et.al[1] ***Heterocyclic Communication*** 2013,19(3), 215-218.



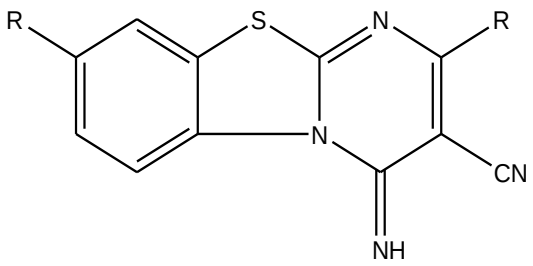
- Synthesis and some novel reactions of 8-chloro-2H-[1,2,4] triazino [3,4-b][1,3] benzothiazole-3,4-dione and 6-chloro-2-hydroazino-1,3-benzothiazole
  Journal of chemical research 2005 October, 632-635,
  S. V. Kuberkar and et.al[2].



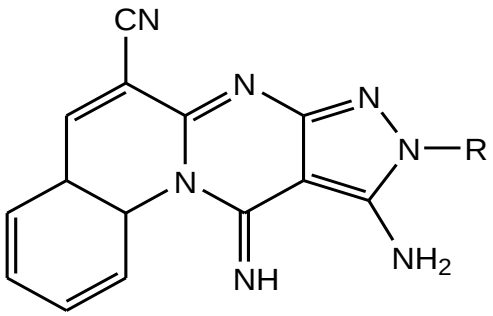
- An efficient synthesis of some novel 3-cyano-4-imino-2-(methylthio)-4H-pyrido [1,2- *a*] pyrimidine and their derivatives, Sambhaji P. Vartale, et al.[2] ***J. Heterocyclic Chem*****,** 2013, 50, 351-355.



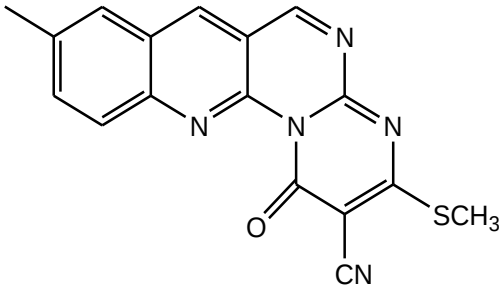
- A convenient synthesis of fused imino pyrimido [2,1-b] benzothiazole and its 2-substituted derivatives **ARKIVOC** 2006 (X) 190-198 S. V. Kuberkar and et. al[1].



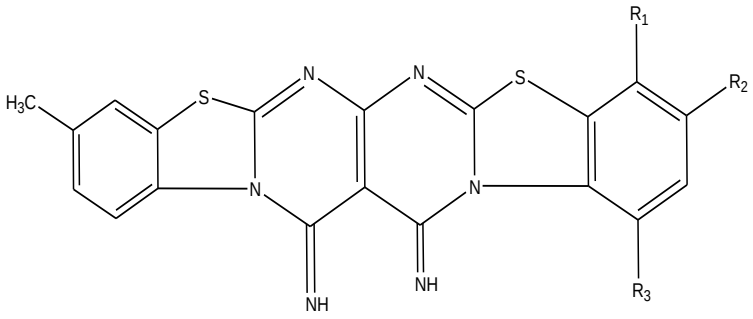
- Synthesis and Antimicrobial Evaluation of 3-amino-11- cyano-4-iminopyrazolo [4, 5-*e*]-4H-pyrimido [2,1-*b*] quinoline and their substituted derivatives. Sambhaji P.Vartale et al.[4] ***Heteroletter***, 2012,2, (1),71-78.



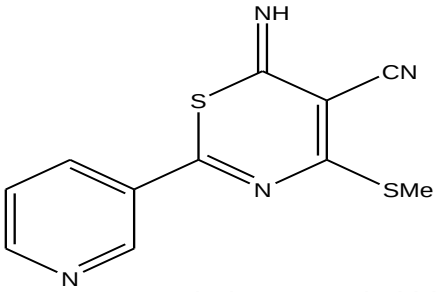
- Convenient one pot synthesis of 3-cyano-9-methylthio-4-oxo-4H-pyrimido[2,1-*b*] quinoline and its reactions with selected nucleophiles, Sambhaji P. Vartale et al.[5] ***Letters in Organic Chemistry***, 2009, 6(7), 544-548.



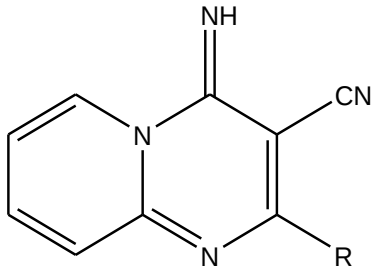
- A Convenient one pot synthesis and antimicrobial activity of 10-methyl-14,15-diimino benzothiazolo[2,3-*b*]pyrimido [5,6-*e*] pyrimido [2,3-*b*]benzothiazole and their substituted derivatives Sambhaji P.Vartale and Sharad V. Kuberkar et al[6] **Journals of *Pelagia Research Library***, 2011, 2(6), 46-51.



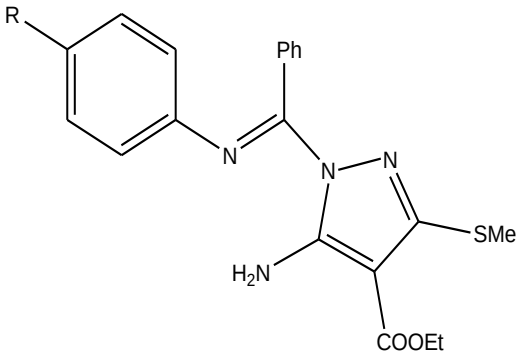
- Synthesis and antioxidant activity of 6-imino-4-(methylthio)-2-(pyridine-3-yl)-6H-1,3-thiazine-5-carbonitrile, Sambhaji P. Vartale et. al[7], **Journals of *International Research Journal of Pharmacy***, DOI: 10.7897/2230-8407.089172.



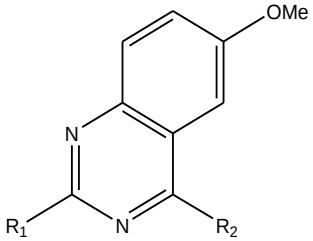
- Synthesis and evaluation of 3-cyano-4-imino-2-methylthio-4H- pyrido [1,2-a] pyrimidine derivatives as potent antioxidant agents. Arabian Journal of Chemistry (2012) xxx, xxx–xxx S.P. Vartale and et.al[5]



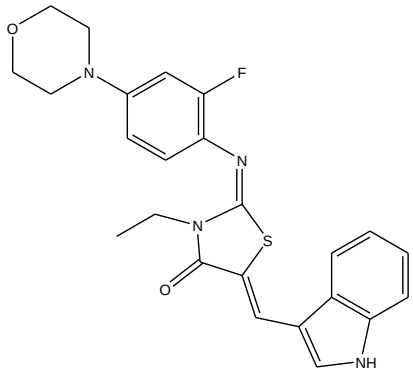
- Reaction of ethyl 2-cyano-3,3- bis(methylthio)acrylate with amidrazones; synthesis of new mercapto pyrazoles and NMR investigation, A.A. Aly, et.al. Journal of Sulfur Chemistry, 2015, Vol.36,2015, issue-5



- Synthesis of Densely Substituted pyrimidine Derivatives. JOC note (**American chemical society**) 2009, 8460-8463. Omar K. Ahmad, and Mohammad Movassaghi et.al.[6]



- DMAP as a versatile and highly efficient catalyst for N-acylation and N- sulphonation of substituted indole
  International Journal of Chemical and Pharmaceutical Sciences 2011, June Vol.2 (2).Vartale S P and et.al[7]



3. Objectives of Research/ Proposed Hypothesis:

- Design synthesis of novel catalytic reagents.
- Extending the research of novel catalytic reagents to new domains, especially targeting the synthesis of different novel imino/oxo fused heterocyclic derivatives.
- Understanding mechanistic details and pathways of novel catalytic reagents.
- Investigate the role of novel catalytic reagents in the activation of substances.
- Establishment of the structure of newly synthesized compounds with help of spectral data.
- Evaluation of physicochemical properties of synthesized novel imino/oxo fused heterocyclic compounds
- Evaluation of biological properties of synthesized novel imino/oxo fused heterocyclic compounds.
- Studying Molecular modeling of synthesized compounds.
- Condensation of novel reagent with synthesized heterocyclic compounds

4. Methodology to be adopted:

- Literature Survey.
- Synthesis of novel catalytic reagents.
- Synthesis and characterization of different imino/oxo fused heterocyclic derivatives by applying novel catalytic reagents.

- Characterization of newly synthesized heterocyclic compounds such as IR, ^{1}H-NMR,

  ^{13}C-NMR, Mass Spectroscopy.
- Evaluation of microbiological activities of synthesized compounds.
- Submission of data to International /National reputed journals for publication.

5. Importance of study/ Society application:

- **International Status:**

Imino/oxo pyrimidine fused heterocyclic derivatives are to possess wide variety of biological properties. These compounds help in preventing many viral, fungal and bacterial diseases with low toxicity. Because of the high efficacy of these compounds, following research groups have recognized the importance of this field and made significant contributions internationally.

1. A. M. El-Agrody
   Department of Chemistry,
   Faculty of Science,
   Al- Azhar Univ. Nasr City,
   Cairo, Egypt

2. N. A. El-Hady
   Department of Chemistry,
   Faculty of Science,
   Al- Azhar Univ. (Girls),
   Nasr City, Cairo, Egypt

3. Sherif M. Sherif,
   Department of Chemistry,
   Faculty of Science,
   Cairo University, Giza 12613,
   Egypt.

4. Karim M. Elsawy,

   National Organization for
   Drug Control and Research
   (NODCAR), P.O. Box 29,
   Cairo, Egypt.

- **National Status:**

Nitrogen, Sulphur, and oxygen-containing heterocycles such as pyrimidine, pyrazole, imidazole, quinoline benzothiazole, and Pyrazole have been widely used in drug molecules these compounds act as antiviral, antifungal, anti-HIV,

anticancer, antioxidant, anti-inflammatory agents with low toxicity. Because of the high efficiency of these compounds, the following research groups have recognized the importance of this field and made significant contributions nationally.

1. **Dr. A. T. Bigu**
Organic Chemistry Division,
National Chemical Laboratory,
Pune, India

2**. Dr. N. T. Patil**
Organic Chemistry Division II,
Indian Institute of Chemical Technology,
Hyderabad-500 007, India

3. **Dr. D. S. Reddy**
Organic Chemistry Division,
National Chemical Laboratory,
Pune, India

4. **Prof. M.S. Shingare,**
Department of Chemistry,
Dr.B.A.M.U. Aurangabad, India.

- **Significance of the study:**

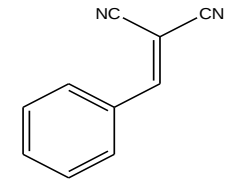
The investigation of novel antimicrobial drugs is an area characterized by vigorous exploration with the goal of overcoming the occurrence of multiple drug resistance. Fused heterocyclic rings like pyridine, pyrimidine, quinoline, thiazole, pyrazole, and benzothiazole, were found to be biologically active compounds.

A fused heteroaromatic group containing sulfur, nitrogen, oxygen, etc atoms plays an important role as the heteroaromatic is incorporated into the structure of many pharmaceuticals.

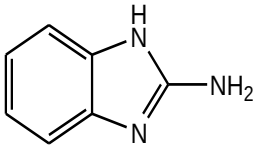
6. Proposed work plan/ Formulation and structure of study:

a) Synthesis of amino heterocycles and reagents: (Ist Year)

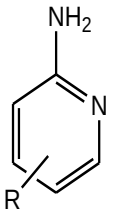
In the proposed research work we plan to synthesize different ketene dithioacetals and different substituted amino heterocycles containing sulfur, nitrogen, and oxygen as heteroatom.



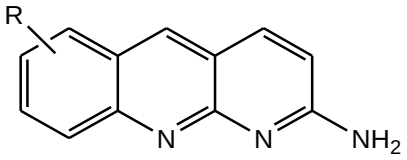
2-benzylidenemalononitrile



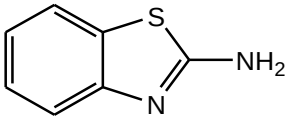
Substituted 2-Amino Benzimidazole



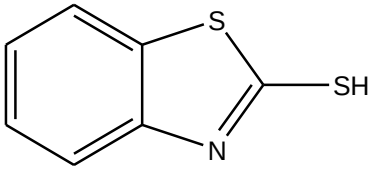
Substituted 2-amino pyridine



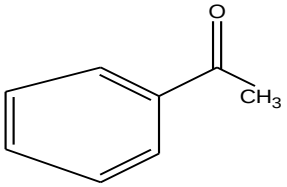
Substituted benzoquinolin-2-amine



Substituted 2-amino benzothiazole



Benzothiazole-2-thiol



1-Phenyl-ethanone

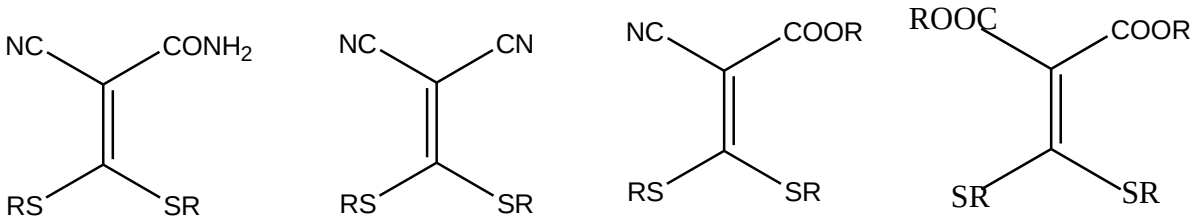
b) Condensation of synthesized amino heterocycles with different reagents: (IInd year)

The synthesized amino heterocycles which contains more than one hetero atom as hetero atom condensation with reagents like guanidine hydrochloride, thiourea, and urea to synthesize main heterocyclic compounds.

Synthesized parent compounds treated with different substituted aniline, phenol, heterylamine, and active methylene compound will give new heterocyclic derivatives.

The above new parent pyrimido compound condensed with a compound containing nitrogen atoms like hydrazine hydrate, Hydrazeno heterocycles, and carbonyl compounds to obtain new fused pyrazolo series derivatives.

Purification of synthesized compounds by using crystallization and conformation of the structure by using spectral data.



c) Evaluation of Physicochemical Parameters: (IIIrd Year)

The physicochemical study of heterocyclic compounds has a very wide scope as this study can demonstrate how our synthesized compounds affect physical properties such as solubility, density, viscosity, and refractive index. Study of Molecular modeling of the The above newly synthesized compounds are to be screened for their pharmacological properties like antioxidant, antimicrobial, antimalarial, antifungal, antituberculosis, anticancer, anti-inflammatory, etc.

Hence, the present research work aimed to **"Synthesis, Chemistry and Characterization of New Fused Heterocyclic Compounds and Study of Their Biological Properties"**

newly synthesized compound. Molecular modeling is **an efficient way of studying protein-protein interactions**. It provides detailed information about how protein residues interact with each other at the atomic level. Molecular docking is **a technique that predicts the preferred orientation, affinity, and interaction of a ligand in the binding site of a protein**.

d) Evaluation of Biological Activity: (IIIrd Year)

Evaluation of biological activity like antibacterial, antifungal and antituberculosis.

Hence, the present research work aimed "Design, Synthesis and Chemistry of fused heterocyclic compounds with evaluation of their pharmacological activities"

References:

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3. Sambhaji P. Vartale, et al.[2] ***J. Heterocyclic Chem*****,** 2013, 50, 351-355.
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6. Sambhaji P. Vartale et al.[5] ***Letters in Organic Chemistry***, 2009, 6(7), 544-548.
7. Sambhaji P.Vartale and Sharad V. Kuberkar et al[6] **Journals of *Pelagia Research Library***, 2011, 2(6), 46-51.
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Miss. Archana P. Mitake
(Research Scholar)
Dept. of Chemistry,
Yeshwant Mahavidyalaya,
Nanded-431602

Dr. Sambhaji P. Vartale
Professor
(Research Guide)
Dept. of Chemistry,
Yeshwant Mahavidyalaya,
Nanded-431602